

ABSTRACT

5 The present invention provides methods of modifying a biological molecule by C-O bond formation utilizing a type II polyketide synthase (PKS) system from the nonactin biosynthesis gene cluster. The type II PKS responsible for biosynthesis of the macrotetralide nonactin includes polypeptides encoded by the *nonJK* genes. The NonJ and NonK polypeptides have been identified by the inventors as ketoacyl synthases
10 capable of directly catalyzing C-O bond formation between substrate molecules. This invention increases the scope and diversity of chemical syntheses available for drug design and combinatorial biosynthesis.

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